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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/920,272	08/22/1997	FREDA MILLER	CIBT-P01-120	8297

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EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	32

DATE MAILED: 03/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/920,272	MILLER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,33,38,41-47 and 49-63* is/are pending in the application.

4a) Of the above claim(s) *61-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,33,38,41-47 and 49-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *29* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 32-33, 38, 41-44, 47, 49, 56, 60 were amended in Paper No. 31, 31, 12/28/2001. Claims 61-63 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 32-33, 38, 41-47, 49-60 are under consideration.

Claim Rejections - 35 USC § 101

Claims 32-33, 38, 41-47, 49 stand rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, for reasons of record set forth in Paper No. 26, 8/30/2001, also see *infra*. As written, claim 49 is directed to naturally occurring stem cells of a mammal, i.e. a product of nature. Amending the claim to encompass isolated cells that do not occur in nature would obviate this rejection.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-33, 38, 41-42, 49-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed: a "cellular composition" of stem cells.

Applicant's amendment, in Paper No. 31, 12/28/2001 and Paper No. 25, 7/11/2001, does not provide sufficient direction for the written description for the above mentioned limitations of claims 32-33, 38, 41-42, 49-60. The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide direction for the instant sequence encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.

Claims 32-33, 38, 41-47, 49-63 are rejected under 35 U.S.C 112, first paragraph, because the specification, while being enabling for neuronal progenitor/precursor cells, does not reasonably provide enablement for stem cells, for reasons of record set forth in Paper No. 26, 8/30/2001. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim.

The basis of the rejection is that claims 32-33, 38, 41-47, 49-63 are overly broad in the recitation of "stem cells". There is insufficient guidance provided in the specification as to how one of ordinary skill in the art would generate stem cells, when the Specification provides methods for producing neuronal progenitor/precursor cells. The cells described in the Specification retained the ability to differentiate into neuronal cells, but there was no demonstration of the cells retaining the ability to differentiate into any other type of cell.

Applicant cites Pereira et al. for the proposition that the work in other cell lines demonstrate that the claimed cells would retain the ability to differentiate into any type of cell. However, Pereira teaches that marrowe contains mesenchymal precursor cells, which may differentiate into fibroblastsic cells, adipocytes and osteogenic cells when cultured under the appropriate conditions. Which supports the rejection, as the specification insufficiently describes the conditions under which the claimed cells could differentiate into any other type of cell, than the demonstrated neuronal cells. Thus it is overly broad to refer to the claimed cells as "stem cells" when the cells are only demonstrated to be neuronal progenitor/precursor cells, and the art clearly teaches that precursor cells have limited fates.

Applicant further argues that addition of the term "neuronal" stem cell to the claim would not further limit the claim. However, the use of the term "stem cell" to describe the claimed cells is clearly not enabled, when the cells have only been demonstrated to be neuronal progenitor/precursor cells.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-33, 38, 41-47, 49-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-33, 38, 41-42, 49-60 are vague and indefinite in the recitation of the term "cellular composition" since there is no definition in the disclosure regarding this limitation. It is not clear whether the term "cellular composition" refers to a mix of cells only, a single type of cells in a carrier, or a cellular extract, therefore the metes and bounds of the claims cannot be determined. Claims 43-47 are rejected insofar as they depend on the recitation of the term "cellular composition".

Claim Rejections - 35 USC § 102

Claims 49-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Avoli et al. (1994) , for reasons of record set forth in Paper No. 26, 8/30/2001.

The rejection set forth that Avoli et al. teaches a method of measuring the spontaneous synchronous field potentials of negative polarity in the presence of 4-AP (page 657, Figure 1), using human brain slices. The brain slices (page 656, first column, third paragraph) can be considered purified cellular compositions, because they comprise many different types of cells, and are isolated from their in vivo milieu.

Applicant argues that the amendment of claim 49 to recite that the stem cells are a cellular composition of stem cells distinguishes the claims over Avoli et al. However, the term cellular composition is unclear, encompassing as it does a mix of cells only, a single type of cells in a carrier, or a cellular extract (see *supra*). Assuming the term "cellular composition" referes to two or more types of cells, Avoli still anticipates the indicated claims, because the brain slices encompass many types of cells.

Applicant further argues that the cells taught by Avoli et al. are not isolated from the microarchitecture and vast array of other cells contained in the slices. However, the cells are isolated from the rest of the brain, and are a cellular composition of stem cells of a mammal.

Claims 32, 38, 43-47, 49, 53-57 and 59-60 are rejected under 35 U.S.C. 102(a) as being anticipated by Sosnowski et al. (1995) as evidenced by Bruckenstein et al. (1988), for reasons of record set forth in Paper No. 26, 8/30/2001, Paper No. 18, 12/06/99 and Paper No. 21, 1/3/2001.

As pointed out in the previous Office Action, at issue is whether the cell composition disclosed by Sosnowski et al. comprises cells which inherently meet the limitations set forth in the indicated claims. The cells comprising the composition of Sosnowski et al. were isolated from peripheral tissue, i.e. olfactory epithelium, in a fashion similar to the cells claimed in the instant application. The cells in the composition taught by Sosnowski et al. differentiate to produce neuronal cells, as do the cells of the instant application. The cells in the composition of Sosnowski et al. can be transplanted into the CNS of a mammal, as can the cells of the instant application. The dispositive factor is therefore the tendency of the cells of the instant application to form non-adherent clusters. Applicant argues that pursuant to MPEP 2112, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." However, the cells taught in Sosnowski may form "aggregates", while instant claim 49 recites that the claimed cells have a tendency to "aggregate" and form non-adherent clusters in culture. The Bruckenstein reference was cited to show the effect of culture conditions on cell morphology, and that given the fact that the Sosnowski cells may form "aggregates", and meet the other limitations of the claims, they are indistinguishable from the cells claimed in the instant application, thus the reference is anticipatory.

The rejection of claim 33 and 49 under 35 U.S.C. 102(b) as being anticipated by Mayo et al. (1992) has been reinstated for reasons of record set forth in Paper No. 7, 10/15/1998. The Examiner regrets the inconvenience.

The rejection set forth that since the claim recites "A stem cell of a mammal" it is an inherent property of the tongue in vitro model system to contain stem cells. Tongue falls within the limitation of peripheral tissue, thus claim 33 is anticipated as well. The claim has been amended to recite a "cellular composition of stem cells". Applicant argues that this distinguishes the claims over the Mayo reference because the cellular composition of Mayo does not teach the cells isolated from the context of various other cell types and the cytoarchitecture of the tissue explant. However, the claim only requires that the cellular composition be "isolated from said peripheral tissue", which the tissue explant clearly is, since it is removed from the tongue. The claim does not recite the limitations that it must be isolated from other cells types or the cytoarchitecture of the tissue explant.

Claim Rejections - 35 USC § 103

Claims 41 and 42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sosnowski et al (1995) in view of La Salle et al. (1993).

The rejection sets forth that the cell compositions taught in Sosnowski et al. comprise cells which are identical to the cells claimed in the instant application, thus it would have been obvious to one skilled in the art at the time the invention was made to use the

adenoviral vector for the transfection of the precursor cells isolated from olfactory epithelium with heterologous genes, including trophic factors. Applicant argues that the cells of the instant claims are distinct from the cells of Sosnowski, and that LaSalle does not teach the transfection of the cells taught by Sosnowski or any stem cell. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

No claim is allowed.

DAVID S. ROMEO
PRIMARY EXAMINER

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
February 27, 2002

DAVID S. ROMEO
PRIMARY EXAMINER